

**SPECIFICATION AMENDMENTS**

Please amend the paragraph beginning at page 2, line 12 and bridging page 3 to page 3, line as follows:

However, studies have revealed that the activity in animals of several samples of marijuana differed significantly, differences which could not be attributed solely to  $\Delta^9$ -THC content (Carlini et al, 1970, *Psychopharmacologia* 18: 82; Karniol and Carlini, 1972, *J Pharm Pharmacol* 24: 833). This led to the hypothesis that other cannabinoid compounds were interfering with  $\Delta^9$ -THC's effects. Specifically, it was shown that CBD was able to block the excitatory effects of  $\Delta^9$ -THC and to ~~potentate~~potentiate the depressant effects of  $\Delta^9$ -THC (Karniol and Carlini, 1973, *Psychopharmacologia* 33: 53) while CBD, administered on its own, had no noticeable effects (Mincis et al, 1973, *Rev Ass Med Brasil* 19: 185). In a further study, Karniol et al (1974, *Eur J Pharma* 28: 172-177) showed that dosages of 15, 30 and 60 mg CBD in admixture with 30 mg  $\Delta^9$ -THC (in orange juice) attenuated several effects of  $\Delta^9$ -THC compared to controls, such as pulse rate acceleration, time production impairment and psychological disturbances. As will be apparent, this corresponds to a CBD: $\Delta^9$ -THC ratio of between 0.5:1 to 2:1. Dalton et al (1976, *Clin Pharmacol Ther* 19: 300-309) observed attenuation of the  $\Delta^9$ -THC effects when both CBD and  $\Delta^9$ -THC were inhaled simultaneously, at 10.5 mg and 1.7 mg respectively (CBD:  $\Delta^9$ -THC ratio of 6:1), but detected no interaction with the pretreatment of CBD. It is important to note that there is also evidence that heating leads to conversion of CBD into  $\Delta^9$ -THC (Mikes and Waser, 1971, *Science* 172: 1158), meaning that the

accuracy of these results must be questioned due to the delivery method used. Zuardi et al (1982, *Psychopharmacology* 76: 245-250) administered 35 mg  $\Delta^9$ -THC and 70 mg CBD in lemon juice (CBD: $\Delta^9$ -THC ratio of 2:1) to volunteers and observed that the anxiety effect associated with  $\Delta^9$ -THC was lessened by CBD but that the tachycardia associated with  $\Delta^9$ -THC was not affected. Based on this result, the authors propose that CBD and  $\Delta^9$ -THC have independent and opposing psychometric effects on man. It is however important to note that the psychometric effects were measured using a "self-rating scale".